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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KOSACK, JOSEPH R

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

11/10/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/529,772	Applicant(s) DENNY ET AL.	
	Examiner Joseph R. Kosack	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,4,8-11,16,19,22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 3,4,8-11,19,22 and 23 is/are allowed.
- 6) ☒ Claim(s) 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 3, 4, 8-11, 16, 19, 22, and 23 are pending in the instant application.

Amendments

The amendment filed on July 23, 2009 has been acknowledged and has been entered into the instant application file.

Previous Claim Rejections - 35 USC § 103

Claims 3, 4, 8-11, 16, and 19 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Friedlos et al. (*J. Med. Chem.* 1997, 1270-1275) in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176).

The Applicant has deleted the non-patentable subject matter, and the rejection is withdrawn in view of the Applicant's traversal.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for ablating tumors with endogenous nitroreductase enzymes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

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In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

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The Nature of the Invention

The nature of the invention is the treatment of tumors that have an endogenous nitroreductase enzyme by administering a compound of claim 4.

The State of the Prior Art and the Predictability or Lack Thereof in the Art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F.2d 833, 166 USPQ

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18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Friedlos et al. (*J. Med. Chem.* 1997, 1270-1275) teach similar compounds to the instant invention for use in GDEPT to treat tumors. However, the results are all drawn to Chinese hamster cell line that are transfected with the exogenous enzyme *E. coli* nitroreductase and not to a cell line with an endogenous nitroreductase enzyme.

The Examiner has been unable to find any teaching in the art as to a tumor cell that contains an endogenous nitroreductase enzyme. Additionally, if there is a tumor cell with an endogenous nitroreductase enzyme, there are no teachings in the art that the Examiner was able to find which teach that the compounds of the instant invention would be activated by the endogenous nitroreductase enzyme.

Hence, in the absence of a showing of tumor cells that contain endogenous nitroreductase enzymes and the ability of those enzymes to activate the compounds of the instant invention, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 4 or any improvement in condition.

The Amount of Direction or Guidance Present and the Presence or Absence of Working

Examples

The specification teaches assays of the compounds with cell lines with exogenous nitroreductase enzymes such as human cytochrome P450 reductase and *E. coli* nitroreductase. However, there are no examples of the compounds of claim 4 being used with an endogenous nitroreductase enzyme.

The Breadth of the Claims

The breadth of the claims is the treatment of all tumors that have an endogenous nitroreductase enzyme by administering a compound of claim 4.

The Quantity of Experimentation Needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which tumors can be treated with the compounds of the instant invention, dosages, the method of drug delivery, and any potential combination therapies.

The Level of Skill in the Art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of formula 1 for the treatment tumors that express an endogenous nitroreductase enzyme, necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of claim 4 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that “ a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling

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disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome deleting the claim.

Conclusion

Claim 16 is rejected. Claims 3, 4, 8-11, 19, 22, and 23 are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph R Kosack/
Examiner, Art Unit 1626